In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below. Please cancel claims 1-37 without prejudice.

38. (Amended) a method for modifying glucose metabolism in a glucose intolerant animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit DPIV-mediated proteolysis with a K_i in the nanomolar or less range.

39. (Amended) A method for modifying glucose metabolism in a glucose intolerant animal, comprising administering to the animal a composition including one or more protease inhibitors which inhibit the proteolysis of glucagon-like peptide 1 (GLP-1) with a K_i in the nanomolar or less range.

40. (Amended) A method for modifying metabolism of a peptide hormone in a glucose intolerant animal, comprising administering to the animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV), wherein the inhibitor inhibits DPIV with a K_i in the nanomolar or less range, in an amount sufficient to increase the plasma half-life of the peptide hormone, which peptide hormone is selected from glucagon-like peptide 2 (GLP-2), growth hormone-releasing factor (GHRF), vasoactive intestinal peptide (VIP), peptide histidine isoleucine (PHI), pituitary adenylate cyclase activating peptide (PACAP), gastric inhibitory peptide (GIP), helodermin, Peptide YY and neuropeptide Y.

41. (Amended) A method for modifying glucose metabolism of a glucose intolerant animal, comprising administering to the animal a composition including a boronyl peptidomimetic inhibitor of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

42. (Amended) The method of claim 41 wherein, the glucose intolerance in the animal is a result of a deletion or disruption of the gene encoding for a glucagon type peptide 1 (GLP-1) receptor.

43. The method of claim 42 wherein, the glucagon type peptide is GLP-1 or GLP-2.

46. (Amended) The method of claim 38, 39, 40 or 41, wherein administering the inhibitor reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.

47. The method of claim 38, 39, 40 or 41, wherein the inhibitor has an EC_{50} for modification of glucose metabolism which is at least one order of magnitude less than its EC_{50} for immunosuppression.

48. (Amended) The method of claim 38, 39, 40 or 41, wherein the inhibitor has an EC_{50} for inhibition of glucose tolerance in the nanomolar or less range.

49. The method of claim 38, 39, 40 or 41, wherein the inhibitor has an EC_{50} for immunosuppression in the μM or greater range.

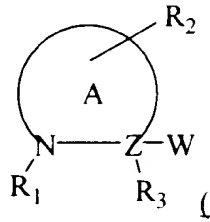
50. The method of any of claim 38, 39, 40 or 41, wherein the inhibitor has a K_i for DPIV inhibition of 0.5 nM or less.

51. (Amended) The method of claim 38, 39, or 40, wherein the inhibitor is peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

52. The method of claim 38, 39, 40 or 41, wherein the inhibitor has a molecular weight less than 7500 amu.

53. The method of claim 38, 39, 40 or 41, wherein the inhibitor is administered orally.

54. (Amended) the method of claim 38, 39, 40 or 41, wherein the inhibitor is represented by the general Formula VII:



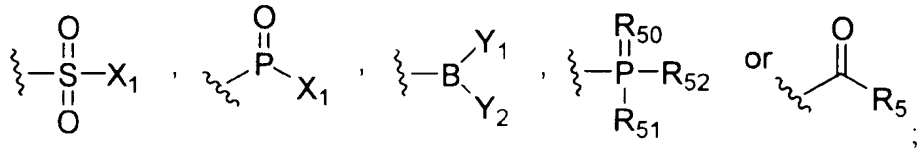
(VII)

wherein,

A represents a 4-8 membered heterocycle including a N and a Cα carbon;

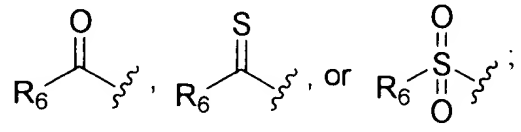
Z represents C or N;

W represents $-CH=NR_5$,



;

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group,



;

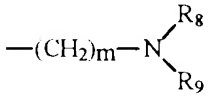
R_2 is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

if Z is N, R_3 represents a hydrogen;

if Z is C, R_3 represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

R_5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-OH$, $-(CH_2)_n-O$-alkyl, $-(CH_2)_n-O$-alkenyl, $-(CH_2)_n-O$-alkynyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_n-SH$, $-(CH_2)_n-S$-alkyl, $-(CH_2)_n-S$-alkenyl, $-(CH_2)_n-S$-alkynyl, $-(CH_2)_n-S-(CH_2)_m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-alkyl, $-(CH_2)_m-O$-alkenyl, $-(CH_2)_m-O$-alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-alkyl, $-(CH_2)_m-S$-alkenyl, $-(CH_2)_m-S$-alkynyl, $-(CH_2)_m-S-(CH_2)_m-R_7$,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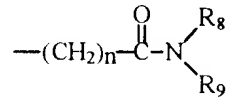
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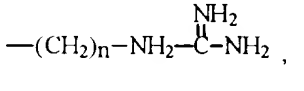
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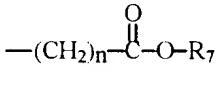

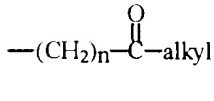
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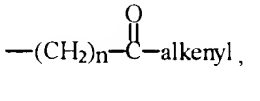
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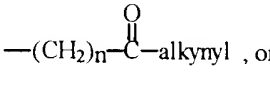
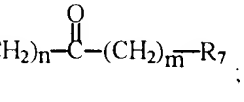

, or

;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or $-C(=O)-(CH_2)_m-R_7$,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{50} represents O or S;

R_{51} represents N_3, SH, NH_2, NO_2 or OR'_7;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X_1 represents a halogen;

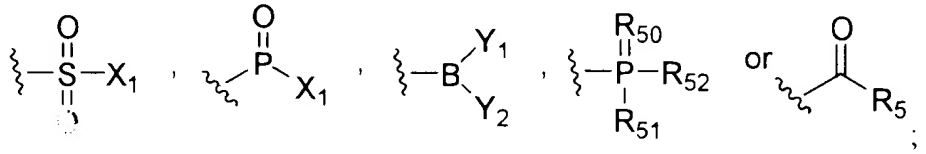
X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

55. (Amended) The method of claim 54, wherein

W represents $-CH=NR_5$,



R_5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-OH$, $-(CH_2)_n-O-alkyl$, $-(CH_2)_n-O-alkenyl$, $-(CH_2)_n-O-alkynyl$, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_n-SH$, $-(CH_2)_n-S-alkyl$, $-(CH_2)_n-S-alkenyl$, $-(CH_2)_n-S-alkynyl$, $-(CH_2)_n-S-(CH_2)_m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

Y_1 and Y_2 can independently or together be hydroxyl, or taken together Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure which is hydrolyzed to hydroxy groups under physiological conditions;

R_{50} represents O or S;

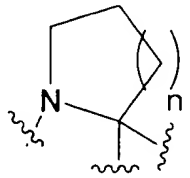
R_{51} represents N_3, SH, NH_2, NO_2 or OR'_7;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X_1 represents a halogen; and

X_2 and X_3 each represent a hydrogen or a halogen.

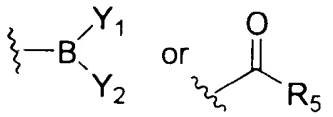
56. The method of claim 54, wherein the ring A is represented by the formula



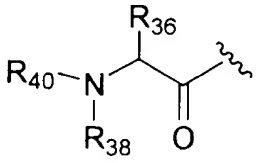
wherein,

n is an integer of 1 or 2.

57. (Amended) The method of claim 54, wherein W represents



58. The method of claim 54, wherein R_1 represents



R_{36} represents a small hydrophobic group and R_{38} is hydrogen, or, R_{36} and R_{38} together form a 4-7 membered heterocycle including the N and the Cα carbon, as defined for A above; and

R_{40} represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group.

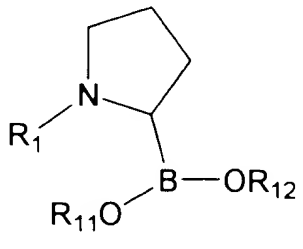
59. The method of claim 54, wherein R_2 is absent, or represents a small hydrophobic group.

60. The method of claim 54, wherein R_3 is a hydrogen, or a small hydrophobic group.

61. The method of claim 54, wherein R_5 is a hydrogen, or a halogenated lower alkyl.

62. The method of claim 54, wherein X_1 is a fluorine, and X_2 and X_3, if halogens, are fluorine.

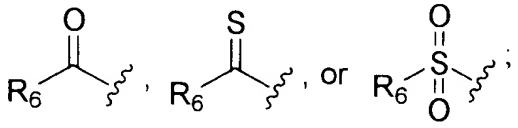
63. The method of claim 54, wherein the inhibitor is represented by the generalFormula (VIII):



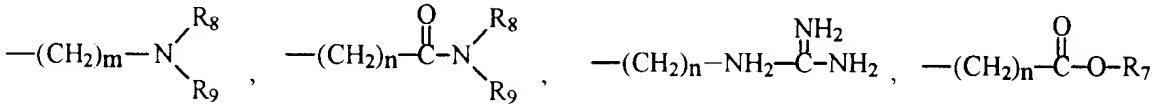
(VIII)

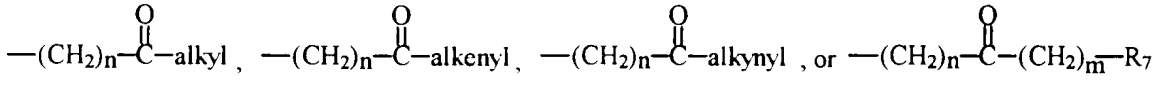
wherein,

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,



R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O-alkyl$, $-(CH_2)_m-O-alkenyl$, $-(CH_2)_m-O-alkynyl$, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S-alkyl$, $-(CH_2)_m-S-alkenyl$, $-(CH_2)_m-S-alkynyl$, $-(CH_2)_m-S-(CH_2)_m-R_7$,





;

R_7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, $-C(=O)-$alkyl, $-C(=O)-$alkenyl, $-C(=O)-$alkynyl, or $-C(=O)-(CH_2)_m-R_7$,

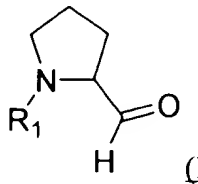
or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{11} and R_{12} each independently represent hydrogen, an alkyl, or a pharmaceutically acceptable salt, or R_{11} and R_{12} taken together with the O-B-O atoms to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

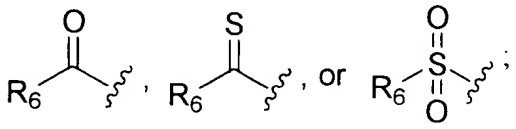
64. (Amended) The method of claim 54, wherein the inhibitor is represented by the general Formula IX:



(IX)

wherein

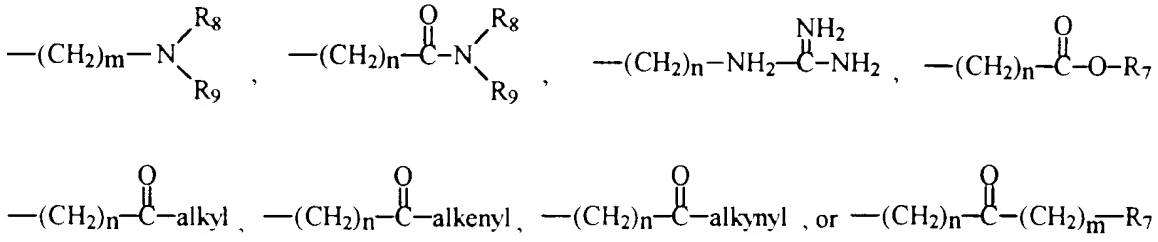
R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog,



;

R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O-alkyl$, $-(CH_2)_m-O-alkenyl$, $-(CH_2)_m-O-alkynyl$, -

$(CH_2)_m$-O-$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, -$(CH_2)_m$-S-$(CH_2)_m$-R_7,



R_7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

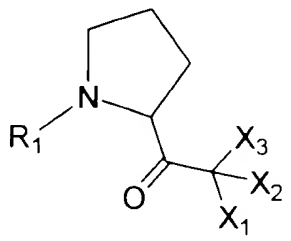
R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, -$(CH_2)_m$-R_7, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-$(CH_2)_m$-R_7,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

m is zero or an integer in the range of 1 to 8; and

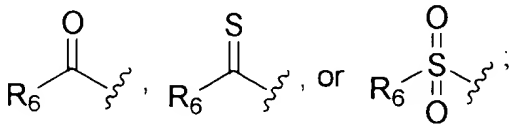
n is an integer in the range of 1 to 8.

65. (Amended) The method of claim 54, wherein the inhibitor is represented by the general formula:

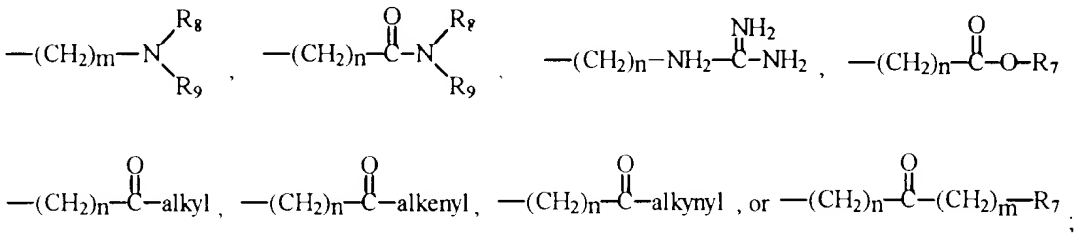


wherein,

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide, or peptide analog,



R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m$-OH, $-(CH_2)_m$-O-alkyl, $-(CH_2)_m$-O-alkenyl, $-(CH_2)_m$-O-alkynyl, $-(CH_2)_m$-O-$(CH_2)_m-R_7$, $-(CH_2)_m$-SH, $-(CH_2)_m$-S-alkyl, $-(CH_2)_m$-S-alkenyl, $-(CH_2)_m$-S-alkynyl, $-(CH_2)_m$-S-$(CH_2)_m-R_7$,



R_7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, $-C(=O)-(CH_2)_m-R_7$, or

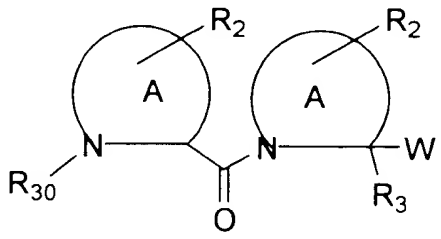
R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

X_1, X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

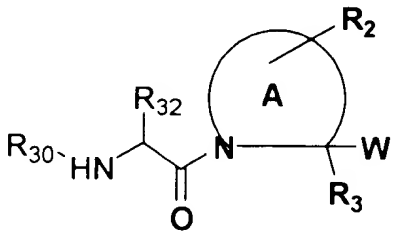
n is an integer in the range of 1 to 8.

66. (Amended) the method of claim 54, wherein the inhibitor is represented by the general Formula Xa or Xb:



(Xa)

or

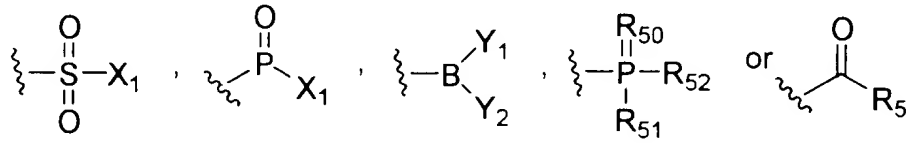


(Xb)

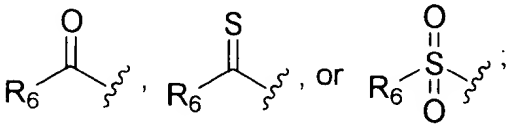
wherein,

A represents a 4-8 membered heterocycle including a N and a Cα carbon;

W represents -CN, -CH=NR$_5$,



R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group,



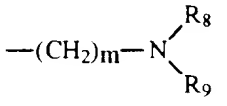
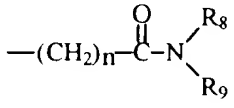
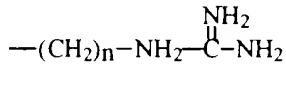
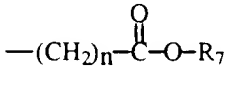
;

R_3 represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -$(CH_2)_m$-R_7, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-lower alkyl, -$(CH_2)_m$-O-lower alkenyl, -$(CH_2)_n$-O-$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-lower alkyl, -$(CH_2)_m$-S-lower alkenyl, or -$(CH_2)_n$-S-$(CH_2)_m$-R_7;

R_5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -$C(X_1)(X_2)X_3$, -$(CH_2)_m$-R_7, -$(CH_2)_n$-OH, -$(CH_2)_n$-O-alkyl, -$(CH_2)_n$-O-alkenyl, -$(CH_2)_n$-O-alkynyl, -$(CH_2)_n$-O-

$(CH_2)_m$-R_7, -$(CH_2)_n$-SH, -$(CH_2)_n$-S-alkyl, -$(CH_2)_n$-S-alkenyl, -$(CH_2)_n$-S-alkynyl, -$(CH_2)_n$-S-$(CH_2)_m$-R_7, -C(O)C(O)NH_2, or -C(O)C(O)OR'$_7$;

R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-R_7, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, -$(CH_2)_m$-S-$(CH_2)_m$-R_7,




R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'$_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, -$(CH_2)_m$-R_7, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-$(CH_2)_m$-R_7,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{32} is a small hydrophobic group;

R_{30} represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group;

R_{50} represents O or S;

R_{51} represents N_3, SH, NH_2, NO_2 or OR'$_7$;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

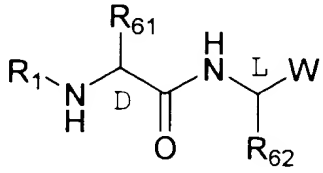
X_1 represents a halogen;

X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

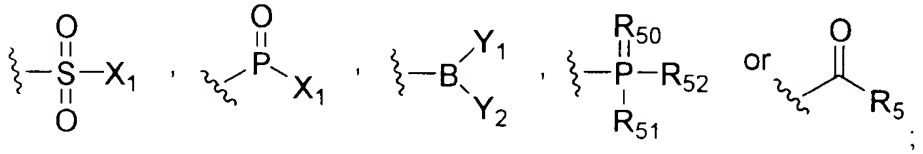
67. (Amended) The method of claim 38, 39, or 40, wherein the inhibitor is represented by the general Formula XI:



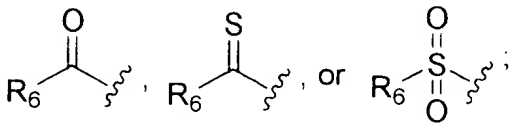
(XI)

wherein,

W represents a functional group which reacts with an active site residue of the targeted protease selected from -CN, $-CH=NR_5$,



R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group, or



R_3 represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

R_5 represents H, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, -(CH2)m-R7, -(CH2)n-OH, -(CH2)n-O-alkyl, -(CH2)n-O-alkenyl, -(CH2)n-O-alkynyl, -(CH2)n-O-(CH2)m-R7, -(CH2)n-SH, -(CH2)n-S-alkyl, -(CH2)n-S-alkenyl, -(CH2)n-S-alkynyl, -(CH2)n-S-(CH2)m-R7, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

R_6 represents a hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-alkyl, $-(CH_2)_m-O$-alkenyl, $-(CH_2)_m-O$-alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-alkyl, $-(CH_2)_m-S$-alkenyl, $-(CH_2)_m-S$-alkynyl, or $-(CH_2)_m-S-(CH_2)_m-R_7$;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_{61} and R_{62}, independently, represent small hydrophobic groups;

Y_1 and Y_2 can independently or together be OH or an alkoxyl, or taken together Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure which is hydrolyzed to hydroxy groups under physiological conditions;

R_{50} represents O or S;

R_{51} represents N_3, SH, NH_2, NO_2 or OR'_7;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X_1 represents a halogen;

X_2 and X_3, independently for each occurrence, represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.